

WHAT IS CLAIMED IS:

1. A method of examining a reactivity of a first sample with a plurality of second samples having different properties from one another, comprising the steps of:

preparing a substrate with said first sample bound thereto in a defined region;

arranging said plurality of second samples within said region independently of one another; and

testing the reactivity of said first sample with each of said second samples.

2. The examination method according to claim 1, wherein said reactivity is a bonding capability between said first sample and said second samples.

3. The examination method according to claim 2, wherein said bonding capability is based on complementation of nucleic acid strands.

4. The examination method according to claim 1, wherein said first sample is originated from an organism, and said second samples have known properties.

5. The examination method according to claim 4, wherein said second samples are synthesized.

6. The examination method according to claim 5, wherein said first sample includes a nucleic acid originated from an organism and having an unknown base sequence, and said second samples include synthesized nucleic acids having known base sequences.

7. The examination method according to claim 6, wherein said first sample includes a set of mRNAs extracted from an organism.

8. The examination method according to claim 6, wherein said first sample includes a cDNA library synthesized based on mRNAs extracted from an organism.

9. The examination method according to claim 4, wherein said first sample includes a nucleic acid originated from an organism and having an unknown base sequence, and said second samples include synthesized chemicals.

10. The examination method according to claim 4, wherein said first sample includes a nucleic acid originated from an organism and having an unknown base sequence, and said second samples include purified proteins.

11. The examination method according to claim 1, wherein said first sample has a known property, and said second samples are originated from an organism.

12. The examination method according to claim 11, wherein said first sample includes a gene having a known sequence.

13. The examination method according to claim 11, wherein said first sample includes a cloned oncogene fragment, and said second samples include nucleic acids originated from an organism.

14. The examination method according to claim 1, wherein said first sample includes a protein fragment extracted from an organism, and said second samples include purified proteins of a single type.

15. The examination method according to claim 1, wherein said first sample includes a purified protein of a single type, and said second samples include protein fragments extracted from an organism.

16. The examination method according to claim 4, wherein said first sample includes a protein fragment originated from an organism, and said second samples include synthesized chemicals.

17. The examination method according to claim 4, wherein said first sample includes a purified protein of a single type, and said second samples include synthesized chemicals.

18. The examination method according to claim 1, wherein said first sample includes a synthesized chemical, and said second samples include nucleic acids extracted from an organism.

19. The examination method according to claim 1, wherein said first sample includes a synthesized chemical, and said second samples include protein fragments extracted from an organism.

20. The examination method according to claim 1, wherein said first sample is comprised of a plurality of samples having different properties, and each of said plurality of

samples is bound to one of partitioned regions forming a matrix on the substrate.

21. The examination method according to claim 20, wherein said first sample includes nucleic acids originated from different biological species, tissues or cells.

22. The examination method according to claim 20, wherein said first sample includes proteins extracted from different biological species, tissues or cells.

23. The examination method according to claim 20, wherein the density of said matrix is 400/cm² or lower.

24. The examination method according to claim 20, wherein an array of spots of said second samples is arranged in each of said partitioned regions in a common arrangement.

25. The examination method according to claim 1, wherein said substrate is made of glass.

26. The examination method according to claim 1, wherein said first sample is fixed on the substrate by electrostatic bonds.

27. The examination method according to claim 1, wherein said first sample is fixed on the substrate by covalent bonds.

28. The examination method according to claim 27, wherein said first sample is bound to said substrate through a chemical reaction of maleimide groups introduced to a glass

surface of the substrate with thiol groups possessed by said first sample.

29. The examination method according to claim 28, wherein said first sample includes a protein, and said thiol groups are cycsteine groups of the protein.

30. The examination method according to claim 28, wherein said maleimide groups are introduced by introducing amino groups to the glass surface and then reacting said amino groups with N-(6-maleimidocaproyloxy)succinimide.

31. The examination method according to claim 28, wherein said maleimide groups are introduced by introducing amino groups to the glass surface and then reacting said amino groups with succinimidyl 4-(maleimidophenyl)butyrate.

32. The examination method according to claim 28, wherein said chemical reaction is a reaction between an epoxy group introduced to the glass surface of the substrate and an amino group possessed by said first sample.

33. The examination method according to claim 30, wherein said amino group is an amino group existing in a nucleic acid base.

34. The examination method according to claim 1, wherein said substrate has a surface previously partitioned by a wall member to define sections forming a matrix, and biological samples having different properties are previously bound to the respective sections as the first sample.

35. The examination method according to claim 34, wherein each of said sections has a hydrophobic wall portion and a hydrophilic bottom portion.

36. The examination method according to claim 35, wherein said wall member has a thickness in the range of 1 to 20 μm .

37. The examination method according to claim 1, wherein said second samples are arranged as spots with a diameter of 200 μm or smaller.

38. The examination method according to claim 1, wherein said second samples are arranged as spots with a density of 400/ cm^2 or higher.

39. The examination method according to claim 1, wherein said second samples are supplied by an ink-jet method.

40. The examination method according to claim 39, wherein said second samples supplied by the ink-jet method include nucleic acids having a base pair length in the range of 2 to 5000 pairs.

41. The examination method according to claim 40, wherein said nucleic acids supplied by the ink-jet method are supplied as an aqueous solution having a concentration in the range of 0.05 to 500 μM .

42. The examination method according to claim 39, wherein said ink-jet method is a bubble jet method.

43. The examination method according to claim 1, wherein each of said second samples is supplied by contacting a pin with a solution of the sample and contacting said pin physically with said substrate.

44. The examination method according to claim 1, wherein each of said second samples is supplied by sucking a solution of the sample using a capillary and then contacting the tip of said capillary physically with the substrate.

45. A method of detecting a complex formed between an oligonucleotide of which base sequence is known and a component having a capability of binding to said oligonucleotide, comprising the steps of:

preparing at least one oligonucleotide of which base sequence is known;

preparing at least two liquid test samples potentially containing a component having a capability of binding to said oligonucleotide;

binding said oligonucleotide as a probe to a predetermined region on a solid substrate to produce a detection substrate;

arranging a plurality of spots of said test samples at a predetermined amount to form an array of said test samples within said region with said oligonucleotide bound thereto;

detecting whether a complex between said oligonucleotide and said component is present or not for each of said plurality of spots; and

determining whether or not said component is contained in each of said liquid test samples, or how strong its binding capability to said oligonucleotide is, based on said detection.

46. The detection method according to claim 45, wherein said oligonucleotide bound to said detection substrate has a base sequence with a base length of 2 to 100.

47. The detection method according to claim 45, wherein said liquid test samples are solutions each containing at least one nucleic acid of which base sequence is unknown, detection is made whether a complex between said oligonucleotide and said nucleic acid is formed or not for each of said test samples to thereby determine whether or not said nucleic acid contains a base sequence complementary to the known base sequence of said oligonucleotide functioning as said component having a capability of binding to said oligonucleotide.

48. The detection method according to claim 47, wherein said nucleic acid contained in each of said liquid test samples includes a set of mRNAs extracted from an organic tissue.

49. The detection method according to claim 47, wherein said nucleic acid contained in each of said liquid test samples includes a cDNA library prepared based on a set of mRNAs extracted from an organic tissue.

50. The detection method according to claim 47, wherein said nucleic acid contained in each of said liquid test samples has a base length of 2 to 5000.

51. The detection method according to claim 45, wherein said liquid test samples are solutions each containing at least

one protein, the proteins contained in said test samples being different from one another.

52. The detection method according to claim 45, wherein said liquid test samples are solutions each containing at least one chemical, the chemicals contained in said test samples being different from one another.

53. The detection method according to claim 45, wherein said liquid test samples are extracts from different biological species, tissues or cells.

54. The detection method according to claim 45, wherein a plurality of oligonucleotides having known base sequences different from one another are used as a probe, and said detection substrate has a plurality of predetermined sections arranged in a matrix form to which said oligonucleotides are to be bound, respectively.

55. The detection method according to claim 54, wherein said plurality of oligonucleotides are bound to said sections to constitute a matrix at a density of $400/\text{cm}^2$ or lower, said sections having the same area as one another.

56. The detection method according to claim 54, wherein said test samples are spotted in an array form in each of said sections to which said plurality of oligonucleotides having known base sequences different from one another are bound so that the spot positions in each section are arranged in the same way as one another.

57. The detection method according to claim 45, wherein said solid substrate used as said detection substrate is made of glass.

58. The detection method according to claim 45, wherein said oligonucleotide is fixed on the detection substrate by covalent bonds.

59. The detection method according to claim 58, wherein said oligonucleotide is fixed on the detection substrate by covalent bonds formed through a chemical reaction of maleimide groups introduced to a glass surface of the substrate used as said solid substrate with thiol (-SH) groups possessed by said oligonucleotide.

60. The detection method according to claim 59, wherein said maleimide groups introduced to the glass surface is formed by first introducing amino groups to the glass surface and then reacting N-(6-maleimidocaproyloxy)succinimide with the amino groups.

61. The detection method according to claim 59, wherein said maleimide groups introduced to the glass surface is formed by first introducing amino groups to the glass surface and then reacting succinimidyl 4-(maleimidophenyl)butyrate with the amino groups.

62. The detection method according to claim 58, wherein said oligonucleotide is fixed on the detection substrate by covalent bonds through a chemical reaction of epoxy groups introduced to a glass surface of the substrate used as said

solid substrate with amino groups possessed by said oligonucleotide.

63. The detection method according to claim 45, wherein said detection substrate has a surface previously partitioned to form a plurality of sections, and two or more different types of oligonucleotides of which base sequences are known are previously bound to the sections, respectively, in a matrix form.

64. The detection method according to claim 63, wherein said sections previously formed on the surface of said detection substrate are separated from each other by a wall member and each section having a hydrophobic wall portion and a hydrophilic bottom portion section is hydrophilic.

64. The detection method according to claim 64, wherein said wall member has a thickness in the range of 1 to 20 μm .

66. The detection method according to claim 45, wherein each of the spots of said two or more test samples formed in each section has a diameter of 200 μm or lower.

67. The detection method according to claim 45, wherein the spots of said two or more test samples formed in each section is arranged at a density of $400/\text{cm}^2$ or smaller.

68. The detection method according to claim 45, wherein each of the spots of said two or more test samples is formed by supplying a predetermined amount of a solution of said test samples by an ink-jet method.

69. The detection method according to claim 68, wherein said two or more test samples are spotted by an ink-jet method as a solution containing a nucleic acid with base length of 100 to 5000, respectively.

70. The detection method according to claim 69, wherein said two or more test samples are spotted by an ink-jet method as a solution containing a nucleic acid as a total concentrations of 0.05 to 500 μM , respectively.

71. The detection method according to claim 69, wherein said ink-jet method used for spotting is a bubble jet method.

72. The detection method according to claim 45, wherein the spots of test samples are formed by contacting a pin having a tip for collecting sample solutions with a solution of each test sample to allow the sample solution to adhere to the tip of said pin for taking a predetermined amount of the solution and then physically contacting the tip of said pin with a surface of the substrate to transfer said predetermined amount of the solution to the substrate surface.

73. The detection method according to claim 45, wherein the spots of test samples are formed by sucking a solution of each test sample using a capillary having a tip for sucking sample solutions thereinto and then physically contacting the tip of said capillary with a surface of the substrate to transfer a predetermined amount of the solution to the substrate surface.